Original Research

Sex Differences Regarding the Impact of Physical Activity on Left Ventricular Systolic Function in Elderly Patients with an Acute Coronary Event

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Introduction: Regular physical activity has been associated with less severity of an acute coronary syndrome (ACS), lower in-hospital mortality rates, and an improved short term prognosis. This study evaluated the relationship between physical activity status and the development of left ventricular systolic dysfunction (LVSD) according to inflammation and sex in elderly patients who had had an ACS.

Methods: We analyzed prospectively collected data from 355 male (age 74 ± 6 years) and 137 female (76 ± 6 years) patients who were hospitalized with an ACS. LVSD was evaluated by echocardiography on the 5th day of hospitalization and physical activity status was assessed by a self-reported questionnaire. Inflammatory response was evaluated by measuring C-reactive protein levels. Logistic regression models were applied to evaluate the effect of physical activity status on the development of LVSD and inflammatory response at entry.

Results: Physical inactivity had a higher prevalence in women who developed LVSD than in the female patients with preserved systolic function (46% vs. 20%, p=0.02). There was a significant positive association between physical activity levels and ejection fraction in women (p=0.06), but not in men (p=0.30). Multi-adjusted logistic regression showed that women who were physically active had 76% lower odds (95%CI: 1-94%) of developing LVSD compared to their sedentary counterparts. Furthermore, physical activity was inversely associated with C-reactive protein levels in both sexes (p=0.08).

Conclusions: Long-term involvement in a physically active lifestyle seems to confer further cardio-protection by reducing the inflammatory response and preserving left ventricular systolic function in elderly female, but not male patients with an ACS.

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Regular physical activity and exercise training offer substantial protection in terms of primary and secondary prevention of coronary artery disease (CAD).[1] The beneficial effects on mortality are observed regardless of age and sex.[2] These effects are mediated through many mechanisms, including favorable alteration of traditional cardiovascular risk factors,[3-7] which in turn reduces cardiovascular morbidity and mortality.

However, the modification of the traditional risk factors cannot explain the full spectrum of the effect of physical exercise on cardiovascular morbidity and mortality.[8] Other potential mechanisms through which physical exercise might act are: improvement of endothelium-dependent vasodilatation, in both epicardial and resistance vessels;[9] improvement in myocardial antioxidants as protective mediators against ischemia-reperfusion injury;[10,11]

an increase in the total cross-sectional area of the coronary vascular bed;[12] a decrease in inflammatory/thrombotic biomarkers;[8] and an increase in cardiac heat shock proteins,[13] endoplasmic reticulum stress proteins,[14] sarcolemmal and mitochondrial ATP-sensitive potassium channels.[15,16] These mechanisms might explain the exercise-induced preconditioning of the heart that protects against serious ischemia/reperfusion injuries.

There are only limited data evaluating the role of physical activity in protecting left ventricular systolic function after an acute coronary syndrome (ACS)—especially in the elderly, who are also underrepresented in the majority of studies. Therefore, we sought to address this question by posing the hypothesis that physical activity might have a beneficial role in protecting the heart against systolic dysfunction after an ACS, even in older adults of both sexes. The purpose of this study was to evaluate, in elderly patients hospitalized for an ACS, the impact of long-term physical activity status on the occurrence of left ventricular systolic dysfunction (LVSD), in relation to the level of inflammatory markers at entry.

Methods

Sample

Between May 2006 and March 2009, 355 male (age 74 ± 6 years) and 137 female (76 ± 6 years) patients, who were hospitalized in our institution for an ACS (first or recurrent) and were ≥65 years old, were enrolled in this study; patients who refused to provide the requested information or died during the first 48 hours of hospitalization were excluded (participation rate 80%). Patients with acute or chronic inflammatory diseases (e.g. cancer, infections) were also excluded. Power analysis (Power and Precision V4) showed that the number of enrolled participants was adequate to evaluate a 15% difference between the percentage of males and females that are active (or inactive) and develop LVSD, achieving a statistical power equal to 80% at the 5% significance level.

Bioethics

The study was carried out in accordance with the Declaration of Helsinki (as revised in 2000) of the World Medical Association and was approved by the Medical Research Ethics Committee of the First Cardiology Clinic of Athens Medical School. All patients were informed about the aims and procedures of the study and gave their consent.

Study design

Clinical, observational study, with in-hospital follow up.

Diagnosis of ACS and LVSD

At entry, a 12-lead electrocardiogram was performed and clinical symptoms were evaluated in all patients by a cardiologist. Blood tests were performed to detect evidence of myocardial cell death (i.e. troponin I and the MB fraction of total creatinine phosphokinase). Acute myocardial infarction (MI) was defined according to guidelines based on electrocardiographic findings and the aforementioned blood tests,[17] while unstable angina was defined by the occurrence of one or more angina episodes at rest within the preceding 48 hours, corresponding to class III of the Braunwald classification.[18] The systolic function of the left ventricle was evaluated from the 2D two- and four-chamber view measurements of the end-diastolic and end-systolic volumes of the left ventricle, using a Hewlett Packard 5500 Sonos with a multifrequency transducer (2.5-4 MHz). Those measurements were actualized at entry and repeated before discharge. LVSD was defined as an ejection fraction below 40% at discharge, according to the European Society of Cardiology's guidelines for the diagnosis and treatment of acute heart failure.[19]

Clinical and biochemical measurements

A detailed medical history was recorded, including previous hospitalization for CAD, history and management of hypertension (defined as systolic and/or diastolic blood pressure >140/90 mmHg or use of antihypertensive medication), hypercholesterolemia (defined as fasting serum total cholesterol >200 mg/dL or use of lipid lowering agents), and diabetes mellitus (defined as fasting glucose >125 mg/dL or use of special treatment), as well as patients' medical family history of CAD. In addition, the clinical course of all patients during hospitalization was recorded, including the performance of revascularization and the time delay from the onset of symptoms to arrival at the hospital. In addition to the clinical information, white blood cell count (WBC) was measured at the time of hospital admission and C-reactive protein (CRP) lev-

els were measured by nephelometry during the first 12-18 hours of hospitalization. Total and high-density lipoprotein cholesterol, blood glucose, and triglycerides were also measured in all participants at the time of hospital admission, using a colorimetric enzymic method in a Technicon automatic analyzer RA-1000 (Dade-Behring Marburg GmbH, Marburg, Germany). Renal function was evaluated using the baseline creatinine clearance rate (CrCl), calculated using the Cockcroft-Gault formula: CrCl = (140 - age) × weight / (72 × serum creatinine) for men, while for female sex, the result of the above equation was multiplied by 0.85. The biochemical evaluation was carried out using standard methods in the same laboratory, following the criteria of the World Health Organization Lipid Reference Laboratories. Samples were processed immediately for the determination of all biochemical parameters.

Demographic, anthropometric and lifestyle characteristics

Sociodemographic characteristics included age and sex. Height and weight were measured to the nearest 0.5 cm and 100 g, respectively. Body mass index was calculated as weight (in kilograms) divided by the square of height (in meters). Obesity was defined as a body mass index greater than 29.9 kg/m^2. To evaluate the physical activity status of the patients during the past year, a modified version of a self-reported questionnaire provided by the American College of Sports Medicine was used.[20] Based on this questionnaire the frequency (times per week), duration (in minutes per time), and intensity of sports or leisure-time physical activity was evaluated. Attention was given to all kinds of activities (e.g. brisk walking, fishing, jogging, running, swimming, biking, etc.) that lasted at least 10 minutes, since this is the minimum required to achieve a health benefit.[21] Patients who did not report any physical activities exceeding this threshold, or reported doing such activities only rarely, were defined as sedentary. All others were defined as active. Current smokers were defined as those who smoked at least one cigarette per day or had stopped cigarette smoking during the past 12 months.

Statistical analysis

Normally distributed continuous variables are presented as mean values ± standard deviation, skewed variables are presented as median and interquartile range, while categorical variables are presented as relative (%) frequencies. Associations between normally distributed continuous variables and patient groups were evaluated using Student's t-test, after controlling for equality of variances (homoscedacity) using the Levene test. The associations between skewed variables (i.e. troponin I, glucose and CRP levels) and patient groups were evaluated using the Mann–Whitney or Kruskal–Wallis tests. Significant linear trends between variables were evaluated using the Jonckheere–Terpstra test. Pairwise comparisons were also performed between groups and p-values were corrected for the inflation of type-I error using the Bonferroni rule. Normality was evaluated by the Shapiro–Wilk test. Associations between categorical variables were tested using the chi-squared test, without the correction for continuity. Binary logistic regression models evaluated the association between patients' characteristics and the occurrence of LVSD. Variables entered in all multi-adjusted models were those that showed a significant association (i.e. p-values <0.1) on the exploratory analyses, or those that were considered as potential confounders in the relationships being investigated (i.e. diagnosis of MI or unstable angina, revascularization at hospital entry, obesity, history of diabetes mellitus, hypertension or hypercholesterolemia, family history of CAD, glucose and troponin I levels, creatinine clearance). Forcing the interaction between continuous variables and their log into the logistic regression models was used to test for linearity of the logit, while collinearity diagnostics (i.e. VIF) were used to test for multicollinearity. Appropriate tests for goodness of fit (i.e. Hosmer–Lemeshow) were applied in all regression models. All hypotheses tested were two-sided and statistical calculations were performed using the PASW Statistics version 18.0 software (SPSS Inc, Chicago, Il, USA).

Results

Incidence of LVSD in ACS patients during hospitalization according to sex

In Table 1 various lifestyle and behavioral characteristics of the female patients are presented according to the development of LVSD. More women with preserved left ventricular systolic function were physically active (p=0.02). Moreover, for elderly women the odds of preserving left ventricular systolic function after an ACS were 3.53-times higher if they had been physically active than if they had been completely inactive.

Table 1. Descriptive characteristics of the patients according to the development of left ventricular systolic dysfunction.

Females	Preserved left ventricular systolic function (n=72)	Left ventricular systolic dysfunction (n=65)	p
Age (years)	74 (9)	78 (11)	0.01
BMI (kg/m^2)	25.8 (5.8)	28.1 (6.5)	0.19
Obesity	23%	29%	0.51
Diagnosis of MI	71%	81%	0.20
STEMI	43%	55%	0.06
Thrombolysis	27%	13%	0.05
First ACS event	76%	72%	0.68
Time from pain onset to hospital (min)	120 (150)	180 (570)	0.02
Left ventricular ejection fraction (%)	50 (11)	35 (11)	<0.001
Previous history of CAD	24%	28%	0.69
Family history of CAD	56%	27%	0.001
Troponin I at entry (ng/mL)	0.3 (3.9)	1.7 (10.8)	0.04
Revascularization	32%	17%	0.06
WBC (count)	9070 (4160)	9470 (5115)	0.10
C-reactive protein (mg/L)	9.2 (30.9)	23.5 (59.1)	0.02
BNP (pg/mL)	321 (471.7)	496.5 (1168.4)	0.06
Total cholesterol (mg/dL)	203.5 (75)	185.5 (66)	0.03
LDL- cholesterol (mg/dL)	121 (50)	112 (58)	0.04
Glucose at entry (mg/L)	133 (138)	156 (82)	0.25
Creatinine clearance (mL/min)	56.4 ± 17.9	45.6 ± 21.4	0.002
Current smoking	17%	19%	0.82
Physical activity	80%	54%	0.02
Years of exercise	7 (20)	0 (8)	0.02
Exercise duration (min)	20 (30)	0 (30)	0.10
Hypertension	77%	84%	0.38
Diabetes mellitus	43%	44%	0.86
Hypercholesterolemia	63%	62%	1.00
Males	**Preserved left ventricular systolic function (n=170)**	**Left ventricular systolic dysfunction (n=185)**	**p**
Age (years)	74 (7)	75 (9)	0.07
BMI (kg/m^2)	27.0 (4.2)	26.7 (4.7)	0.52
Obesity	22%	21%	0.88
Diagnosis of MI	69%	85%	<0.001
STEMI	39	48%	0.06
Thrombolysis	27%	23%	0.27
First ACS event	50%	61%	0.04
Time from pain onset to hospital (minutes)	90 (146)	90 (225)	0.32
Left ventricular ejection fraction (%)	50 (10)	35 (10)	<0.001
Previous history of CAD	50%	39%	0.04
Family history of CAD	31%	30%	0.90
Troponin I at entry (ng/mL)	0.3 (2.8)	1.3 (8.8)	<0.001
Revascularization	36%	29%	0.22
WBC (count)	8640 (3410)	9310 (4272)	0.05
C-reactive protein (mg/L)	13.4 (30.6)	21.4 (61.8)	0.05
BNP (pg/mL)	158.6 (280.1)	364.0 (665.2)	<0.001
Total cholesterol (mg/dL)	169.5 (59)	173.5 (58)	0.89
LDL- cholesterol (mg/dL)	103 (44)	108.5 (43)	0.50
Glucose at entry (mg/L)	133 (70.5)	138 (88.5)	0.37
Creatinine clearance (mL/min)	61.8 ± 22.3	59.5 ± 23.7	0.37
Current smoking	32%	37%	0.43
Physical activity	81%	72%	0.22
Years of exercise (years)	3 (15)	1 (20)	0.74
Exercise duration (minutes)	27 (60)	12 (30)	0.16
Hypertension	70%	66%	0.48
Diabetes mellitus	33%	43%	0.09
Hypercholesterolemia	49%	54%	0.43

Data are presented as median values (interquartile range), mean ± SD, or relative frequencies.

ACS – acute coronary syndrome; BMI – body mass index; BNP – brain natriuretic peptide; CAD – coronary artery disease; LDL – low-density lipoprotein; MI – myocardial infarction; STEMI – ST- elevation MI; WBC – white blood cells.

In women, the family history of CAD seemed to have an important impact on outcome (more likely to preserve systolic function, p=0.001). Additionally, female patients who developed LVSD had higher levels of troponin I, worse kidney function, more delayed arrival at hospital, lower levels of cholesterol and more pronounced inflammatory status (Table 1). As for elderly men, it seems that physical activity was not associated with LVSD development (p=0.22). In contrast, male patients who developed LVSD after the ACS event had higher troponin I levels, were more likely to have a diagnosis of MI, had higher levels of inflammatory markers (i.e. WBC, CRP) and tended to be older than their counterparts who did not develop LVSD (Table 1).

Physical activity and LVSD according to sex

As shown in Table 2, female patients with a greater adherence to physical activity had a higher left ventricular ejection fraction and a lower body mass index compared to those who declared themselves to be completely inactive. It also seems that women who were more physically active tended to present to the hospital having lower glucose and inflammatory markers. Similarly, men who reported higher levels of physical activity (Table 2*)* had lower levels of glucose and CRP at hospital admission.

As stated above, it seems that an inverse relationship exists between physical activity status and left ventricular ejection fraction in elderly female post-ACS patients. Many other variables, such as hospitalization characteristics or features of the patient's history, may be related to the outcome of interest as well as to the physical activity status of the participants and may therefore confound the results. Thus, several possible confounders were entered into multiple logistic regression models in order to evaluate the effect of physical activity on left ventricular ejection fraction. According to this analysis (Table 3), women who were physically active had 76% lower odds (95% CI, 0.01-0.94%) of developing LVSD, compared to their sedentary counterparts. Furthermore, women with a family history of CAD seemed to have 83% lower odds of developing LVSD. MI and revascularization procedures at hospital admission had a substantive impact on the outcome: the former in a positive way (OR for women 5.66, 95%CI: 1.14-28.16; OR for men 3.68, 95%CI: 1.63-8.28) and the latter in a negative one (OR for women 0.14, 95%CI: 0.02-0.80; OR for men 0.76, 95%CI: 0.37-1.55) (Table 3).

Discussion

This study revealed that long-term involvement in a physically active lifestyle downregulates low-grade inflammation in both sexes. This translates into preservation of systolic function in elderly women, but not in elderly men. It is known that the protective effect of exercise is expected to be more pronounced for patients who exercise for longer periods, as there is a graded relationship between increasing levels of activity and decreasing rates of cardiovascular disease.[1,22] It seems that many of the beneficial effects of exercise are due to its favorable downregulation of the low-grade inflammation that is present in atherosclerosis[23, 24] and contributes, as expressed by higher levels of CRP, in an independent way to the deterioration of left ventricular systolic function after an ACS.[25] Existing literature confirms that this effect of exercise in lowering cardiovascular disease risk is mediated by favorable alterations in known risk factors, especially in inflammatory/hemostatic factors and blood pressure.[11] In the case of ACS, physical activity has been associated with a reduced severity of an acute coronary event, reducing in-hospital mortality and improving short-term prognosis.[26] It has been demonstrated that endurance exercise promotes cardioprotection, which is protection of the heart against ischemia-reperfusion injury, as occurs during an acute coronary episode.[27,28] This favorable effect is mediated through several proposed mechanisms. Two of the best documented are higher levels of antioxidants and increased expression of sarcolemmal ATP-sensitive potassium channels, both representing improved cardiac antioxidant capacity. However, several other mediating mechanisms might contribute to exercise-induced cardioprotection, such as the favorable alterations in coronary circulation and endothelial function, induction of myocardial heat-shock proteins, and elevation of endoplasmic reticulum stress proteins.[29] In our study, physically active patients of both sexes had lower glucose levels and inflammatory markers at hospital admission, compared to the physical inactive patients, while an inverse relationship was detected between physical activity status and serum CRP levels at admission.

Regarding possible sex differences in the protective effects of physical activity, the existing literature is inconsistent and controversial. According to Hu et al,[30] moderate and high levels of physical activity lower the likelihood of developing heart failure among both men and women, irrespective of body mass in-

Table 2. Lifestyle, behavioral and clinical characteristics of patients with acute coronary syndromes according to exercise status.

Exercise status	Never (n=33)	Rare (n=12)	1-2 times/week (n=7)	3-4 times/week (n=36)	5+ times/week (n=16)	p
			Females			
Age (years)	78 (6)	76 (7)	77 (7)	74 (8)	76 (13)	0.26
BMI (kg/m^2)	28.4 (5.8)	27.3 (6.3)	24.6 (8.3)	26 (5.6)	25 (10)	0.21
Obesity	30%	36%	17%	23%	25%	0.86
Diagnosis of MI	58%	75%	71%	78%	75%	0.45
Left ventricular ejection fraction (%)	40 (10)	49 (20)*	50 (13)*	45 (20)	50 (10)	0.02
First CAD event	51%	83%	86%	72%	75)%	0.13
Family history of CAD	41%	75%	71%	47%	47%	0.23
Troponin I at entry (ng/mL)	0.2 (3.4)	0.7 (4.5)	1.3 (6.2)	0.4 (3.3)	4.2 (9.7)	0.54
WBC (count)	9400 (5260)	9800 (3395)	8400 (4270)	7900 (2890)*	9600 (10900)	0.02
C-reactive protein (mg/L)	29.1 (82)	12.8 (30.9)	12 (50.9)	9.2 (17.7)	10.6 (24.6)	0.52
BNP (pg/ml)	451 (621.6)	277.5 (2317.7)	240.1	502.5 (845)	364.2 (624.4)	0.57
Total cholesterol (mg/dL)	175 (62)	193 (95)	215 (43)	202 (60)	211 (74)	0.36
LDL-cholesterol (mg/dL)	110 (50.5)	115.5 (62.5)	101.5 (81.2)	128 (48)	121 (62)	0.50
Glucose at entry (mg/L)	157 (119)	139 (82)	109 (106)*	123 (46)	151 (109)	0.02
Revascularization	18%	33%	29%	6%	31%	0.09
Creatinine clearance (mL/min)	45.9 ± 24	54.1 ± 9.9	54.1 ± 15.3	54.6 ± 20.2	51 ± 21.5	0.50
Current smoking	21%	17%	14%	17%	25%	0.96
Hypertension	88%	73%	71%	72%	94%	0.25
Diabetes mellitus	61%	33%	43%	29%	44%	0.11
Hypercholesterolemia	66%	54%	57%	59%	53%	0.94
Time from pain onset to hospital (min)	120 (375)	90 (900)	90 (105)	120 (165)	337 (1688)	0.14
			Males			
Age (years)	75 (10)	75 (12)	74 (7)	75 (8)	72 (7)	0.37
BMI (kg/m^2)	27.4 (4.5)	27.5 (5.6)	25.7 (2.5)	26.5 (5.1)	27.1 (4.2)	0.16
Obesity	21%	32%	5%	24%	14%	0.10
Diagnosis of MI	76%	68%	81%	69%	72%	0.73
Revascularization	18%	32%	33%	23%	29%	0.37
Left ventricular ejection fraction (%)	40 (10)	45 (15)	42 (14)	45 (18)	40 (15)	0.18
First CAD event	53%	49%	24%	44%	59%	0.06
Family history of CAD	44%	31%	47%	32%	36%	0.47
Troponin I at entry (ng/mL)	0.7 (4.6)	0.5 (6.1)	0.6 (3.4)	0.2 (4)	0.7 (11.4)	0.70
WBC (count)	8485 (3610)	9000 (3215)	8100 (4367)	8815 (3697)	8250 (3810)	0.74
C-reactive protein (mg/L)	29.2 (64.8)	21 (27.2)	7 (32.1)	12.4 (35.3)*	18.2 (77.2)	0.08
BNP (pg/ml)	387 (697.5)	356 (676.7)	205 (267)	251.5 (326.7)	235.3 (304.7)	0.55
Total cholesterol (mg/dL)	173 (54)	196 (86)	195 (53)	189 (73)	164 (52)	0.04
LDL-cholesterol (mg/dL)	107 (45)	117 (56)	93 (53)	109 (44)	103 (33)	0.10
Glucose at entry (mg/L)	140 (81)	147 (82)	157 (102)	131 (57)	124 (69)	0.17
Creatinine clearance (mL/min)	57.7 ± 24.6	61.8 ± 29	57.6 ± 24.1	60.2 ± 22.2	65.4 ± 16.8	0.28
Current smoking	32%	30%	24%	31%	30%	0.97
Hypertension	78%	73%	71%	62%	57%	0.13
Diabetes mellitus	45%	62%*	25%	32%	35%	0.01
Hypercholesterolemia	46%	62%	68%	44%	60%	0.11
Time from pain onset to hospital (min)	90 (316)	90 (120)	90 (150)	90 (109)	90 (586)	0.97

Data are presented as median values (interquartile range), mean ± SD, or relative frequencies.
*$p<0.05$ between diagnosis group after correcting for multiple comparisons through the Bonferroni adjustment. Abbreviations as in Table 1.

dex values. According to Djoussé et al,[31] regular exercise, among other healthy lifestyle variables, is associated with a lower lifetime risk of heart failure among apparently healthy men. However, the latter study included no data concerning women. On the other hand, according to an NHANES I follow-up study,[32] in the multivariate model lower physical activity was positively associated with the risk of congestive heart

Table 3. Results from multiple logistic regression analysis that evaluated the association between physical activity status and the development of left ventricular systolic dysfunction after an acute coronary syndrome in female and male elderly patients.

Variable	OR (95% CI)		p for sex differences
	Females	Males	
Physical activity (active vs. sedentary)	0.24 (0.06-0.99)	10.36 (0.69-20.69)	<0.001
Myocardial infarction vs. unstable angina	5.66 (1.14-28.16)	30.68 (10.63-80.28)	<0.001
Revascularization at entry (yes vs. no)	0.14 (0.02-0.80)	0.76 (0.37-10.55)	0.05
Glucose levels at entry (per 1 mg/dL)	0.99 (0.98-1.00)	10.00 (0.99-10.00)	0.85
Troponin I at entry (per 1 ng/mL)	1.004 (0.96-1.05)	10.01 (0.99-10.03)	0.01
Creatinine clearance at entry (per 1 mL/min)	0.99 (0.96-1.02)	0.98 (0.96-0.99)	0.50
Obesity (yes vs. no)	1.54 (0.34-6.99)	10.61 (0.66-30.95)	0.53
Hypertension (yes vs. no)	2.13 (0.43-10.45)	0.88 (0.43-10.78)	<0.001
Hypercholesterolemia (yes vs. no)	0.76 (0.22-2.62)	10.25 (0.66-20.39)	<0.001
Diabetes mellitus (yes vs. no)	2.96 (0.63-13.98)	20.85 (10.31-60.20)	0.61
Family history of CAD (yes vs. no)	0.17 (0.05-0.58)	10.44 (0.73-20.85)	<0.001

*log-ORs were compared between sexes using the Z-test.
OR – odds ratio; CI – confidence interval; CAD – coronary artery disease.

failure in women but not in men. Furthermore, in a recent study by Wang et al,[33] the authors found that moderate and high levels of occupational or leisure-time physical activity were associated with a reduced risk of heart failure in both sexes, yet commuting had a significant positive effect only in women.

This study highlights the controversy over the possibly different impact of physical activity on cardiac function according to sex. Questions arise as to the existence of sex differences at the cellular level. In this context a systematic review seems appropriate. According to the literature,[34] there is a gap between men and women in the age at which total CAD manifests, since men start having CAD problems ten years earlier than women.[34] Indeed, our findings suggested that men more frequently had a previous history of CAD ($p<0.001$). It is possible that physical activity may not confer benefits on patients who tend to have more "injured" hearts. Another thing to consider about men is that they engage in more unhealthy lifestyle habits than women (e.g. they smoke more, as supported by our findings; $p<0.001$),[35] which may oppose any benefit that might come from being physically active.

The reported findings, along with the above-mentioned theoretical implications, support the role of exercise in the primary prevention setting. Physical activity, as part of a healthy lifestyle pattern, contributes to the prevention of MI in women.[36] This could strengthen the physician's advice and patients' adherence, stressing the different aspects of exercise's cardioprotection, irrespective of patients' older age or female sex. This is in accordance with the need for establishing the importance of physical activity by every means.[1] Furthermore, exercise provides protection against LVSD and incident heart failure after an ACS.

Limitations

Occupational physical activity was not taken into account in the present study. Another possible source of error is the recall bias. We tried to accurately assess the physical activities of the patients; however, recall bias may still exist, and even to a different degree between men and women, depending, among other things, on the psychological impact of the ACS event. The fact that patients who died in the first 48 hours were not included in the study might confer some bias on the results. However, these patients were estimated as being approximately 4% of the total number of patients and were not, therefore, expected to alter our results significantly.

Conclusions

Long-term involvement in a physically active lifestyle, which means a consistent exercise program that is sufficient in duration and intensity, provides another cardioprotective mechanism, that is, preservation of systolic function after an acute coronary event. This finding appears to be of importance to elderly women. It seems that this is mediated through favorable alterations in inflammatory/thrombotic markers and downregulation of systemic inflammation.

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